

REMARKS

Reconsideration and allowance are respectfully requested.

Claims 6-15 and 20-30 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Support may be found, *inter alia*, at page 6, lines 31-34, of the specification.

Information Disclosure Statement

To satisfy their continuing duties of candor and good faith, Applicants bring to the attention of the Examiner the copending application, Serial No. 10/584,847. In the '847 application, a provisional obviousness-type double patenting rejection was made citing claims in the present application. Therefore, because the other examiner considered the subject matter to be related, Examiner Lau is invited to consider the prosecution history and prior art of the '847 application, which are accessible through the PTO's Image File Wrapper (IFW), in view of the Federal Circuit's holding in *McKesson Information Solutions v. Bridge Medical*, 82 USPQ2d 1865 (Fed. Cir. 2007). To avoid duplication of those materials in the PTO's records, reference to the IFW is encouraged but Applicants would submit copies of these materials for the Examiner's review if he prefers.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See *id.* at 1397

("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. An inquiry is required as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.* at 1396. But a claim that is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 6, 8-11, 13 and 20-29 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa et al. (U.S. Patent 4,303,680) in view of Keller et al. (U.S. Patent 4,623,723) and in view of Amersham Biosciences (*Gel Filtration: Principles and Methods*, pp. 1-34, 2002) and in view of Chae et al. (Bioresource Technol. 76:253-258, 2001), with evidence of Kanegae et al. (U.S. Patent 4,810,509). Applicants traverse.

Applicants' claims 6 and 20 relate to processes to produce compositions containing 5'-ribonucleotides which comprise at least the following:

- (i) treating microbial cells to release the cell contents comprising RNA,
- (ii) separating solid material originating from the microbial cells from soluble material present in the released cell content,
- (iii) separating the RNA present in the released cell contents from other soluble cell material smaller than 50 kDa wherein the other soluble cell material comprises peptides and small proteins, and
- (iv) converting the separated RNA into 5'-ribonucleotides; whereby the process is used to produce a composition containing 5'-ribonucleotides.

Thus, Applicants' process as presently claimed (see claims 6 and 20) contains at least two separation steps: separation step (ii) wherein solid material originating from the microbial cells is separated from soluble material present in the released cell content and separation step (iii) wherein RNA present in the released cell contents is separated

from other soluble cell material smaller than 50 kDa wherein the other soluble cell material comprises peptides and small proteins.

By contrast, Tanekawa's process contains only one separation step, namely step (3) wherein the soluble fraction (containing the extracted RNA) is separated from insoluble residue, which is mainly cell walls of yeast (see column 4, lines 13-15, of the '680 patent). This separation step can be considered to correspond with separation step (ii) of Applicants' claimed process.

Thus, the process according to Applicants' claim 6 or 20 differs from Tanekawa's process in that the presently claimed process contains an additional separation step after the separation of solid material originating from the microbial cells from soluble material present in the released cell content. The effect of this additional and subsequent separation step is that a composition can be produced which contains at least 55% w/w (based on total dry weight matter) of 5'-ribonucleotides (see present specification's Example 1, where the amount of 5'-ribonucleotides in the composition produced is 97% w/w; Example 2, also 97% w/w of 5'-ribonucleotides; and Example 3, 78% w/w of 5'-ribonucleotides).

By contrast, Tanekawa's process includes only one separation step: i.e., separating RNA from insoluble residue. This process produces a composition, however, that is much lower in the content of 5'-ribonucleotides than a composition produced using the process of the claimed invention, namely between 0.17 - 3.55% (see Table I on column 6 and column 7, lines 38-39, of the '680 patent). Because of the nature of RNA, there are always four types of 5'-ribonucleotides present in more or less equal amounts (i.e., 5'-AMP, 5'-GMP, 5'-UMP, and 5'-CMP; 5'-AMP can be converted to 5'-IMP). This means that the total amount of 5'-ribonucleotides in the composition produced by the process disclosed in Tanekawa is at most $4 \times 3.55\% = 14.2\%$, which is substantially lower than what is achieved by the presently claimed process.

Moreover, Keller, Amersham, and Chae cited in the Office Action fail to teach or make obvious using two different separation steps to produce a composition containing 5'-ribonucleotides, let alone that this would result in a composition comprising at least

55% w/w of 5'-ribonucleotides with a reasonable expectation of success. Therefore, claims 6 and 20 are patentable over the cited documents.

Since the combination of Tanekawa, Keller, Amersham, and Chae does not render Applicants' invention as represented by independent claim 6 or 20 unpatentable, claims 8-11, 13 and 21-29 are also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Claims 12 and 30 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa et al. (US 4,303,680) in view of Keller et al. (US 4,623,723) and in view of Amersham Biosciences (2002) and in view of Chae et al. (2001) as previously applied, and further in view of Fernandez et al. (Acta Biotechnol. 12:49-56, 1992). Applicants traverse.

The disclosures of Tanekawa, Keller, Amersham, and Chae were discussed in the first obviousness rejection. Fernandez was cited for allegedly disclosing a preference for ultrafiltration over precipitation for the purpose of purifying intracellular components. Thus, the failure of Tanekawa, Keller, Amersham, and Chae to disclose Applicants' claimed invention as discussed under the first obviousness rejection is not remedied by the attempt to combine their disclosures with Fernandez. The latter document was cited by the Examiner to substitute one purification step for another in the process. It would not have been obvious from the combination of cited documents to perform two different separation steps. Therefore, claims 6 and 30 are patentable over the cited documents.

Since the combination of Tanekawa, Keller, Amersham, Chae, and Fernandez does not render Applicants' invention as represented by independent claim 6 unpatentable, claim 12 is also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claim. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Claims 6 and 14-15 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa et al. (US 4,303,680) in view of Keller et al. (US 4,623,723) and in

view of Amersham Biosciences (2002) and in view of Chae et al. (2001) as previously applied, and further in view of Tsuda et al. (US 4,374,981). Applicants traverse.

The disclosures of Tanekawa, Keller, Amersham, and Chae were discussed in the first obviousness rejection. Tsuda was cited for allegedly disclosing ultrafiltration of fermentation broth for the separation of inosine and/or guanosine to remove high molecular weight substances. Thus, the failure of Tanekawa, Keller, Amersham, and Chae to disclose Applicants' claimed invention as discussed under the first obviousness rejection is not remedied by the attempt to combine their disclosures with Tsuda. The latter document was cited by the Examiner to include ultrafiltration as a purification step in the process. It would not have been obvious from the combination of cited documents to perform two different separation steps. Therefore, claim 6 is patentable over the cited documents.

Since the combination of Tanekawa, Keller, Amersham, Chae, and Tsuda does not render Applicants' invention as represented by independent claim 6 unpatentable, claims 14-15 are also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Claims 6-7 and 25 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa et al. (US 4,303,680) in view of Keller et al. (US 4,623,723) and in view of Amersham Biosciences (2002) and in view of Chae et al. (2001) as previously applied, and further in view of Potman et al. (US 5,288,509). Applicants traverse.

The disclosures of Tanekawa, Keller, Amersham, and Chae were discussed in the first obviousness rejection. Potman was cited for allegedly disclosing deactivation of native enzymes in a yeast extract with a protease. Thus, the failure of Tanekawa, Keller, Amersham, and Chae to disclose Applicants' claimed invention as discussed under the first obviousness rejection is not remedied by the attempt to combine their disclosures with Potman. The latter document was cited by the Examiner to add an inactivation step to the process. It would not have been obvious from the combination of cited documents to perform two different separation steps. Therefore, claim 6 is patentable over the cited documents.

Since the combination of Tanekawa, Keller, Amersham, Chae, and Tsuda does not render Applicants' invention as represented by independent claim 6 unpatentable, claims 7 and 25 are also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Withdrawal of the Section 103 rejections is requested because the claims would not have been obvious to one of ordinary skill in the art when this invention was made.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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